### PATENT COOPERATION TREATY

# **PCT**

#### INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER ACTION	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
042637woMest International application No.	International filing date (day/month/	year) (Earliest) Priority Date (day/month/year)
•••		
PCT/EP2004/053573	17/12/2004	18/12/2003
Applicant		
EVOTEC NEUROSCIENCES GMBH		
This International Search Report has bee according to Article 18. A copy is being tra	n prepared by this International Searcl ansmitted to the International Bureau.	ning Authority and is transmitted to the applicant
This International Search Report consists	of a total of 0.5 shee	ts.
	a copy of each prior art document cite	
Basis of the report     With regard to the language, the language in which it was filed, unl	international search was carried out o less otherwise indicated under this iter	n the basis of the international application in the n.
The international this Authority (Ru		a translation of the international application furnished to
b. With regard to any nucle	otide and/or amino acid sequence d	isclosed in the international application, see Box No. I.
2. Certain claims were fou	nd unsearchable (See Box II).	
3. X Unity of invention is lac	king (see Box III).	
4. With regard to the title,		
X the text is approved as su	ibmitted by the applicant.	
the text has been establis	shed by this Authority to read as follows	s:
5. With regard to the abstract,		
X the text is approved as su		Authority on November 19 Day No. 197. The conditions
the text has been establis may, within one month fro	sned, according to Hule 38.2(b), by this on the date of mailing of this internation	Authority as it appears in Box No. IV. The applicant nal search report, submit comments to this Authority.
6. With regard to the <b>drawings</b> ,		
·	oublished with the abstract is Figure No	
as suggested by		dia annual di ann
· 🖳 ·	is Authority, because the applicant faile	
	is Authority, because this figure better	characterizes the invention.
b. X none of the figures is to b	e published with the abstract.	

International application No. PCT/EP2004/053573

# INTERNATIONAL SEARCH REPORT

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
Claims Nos.:     because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box III Observations where unity of invention is lacking (Continuation of Item 3 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
see additional sheet
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. X  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1, 2, 8, 11, 12, 14, 15, 16
Remark on Protest  The additional search fees were accompanied by the applicant's protest.  No protest accompanied the payment of additional search fees.

#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1,2,8,11,12,14,15,16

The underlying inventive concept of these claims is the connection between altered levels of HIF3alpha levels and neurodegenerative disorders.

2. claims: 3,10

Kits for the determination of the levels of  ${\tt HIF3alpha}$  in samples.

3. claims: 4-8

Transgenic non-human animals with a non native HIF3alpha sequence.

4. claims: 9,13

 ${\tt Methods\ of\ identifying\ modulators\ of\ HIF3alpha}$ 

#### INTERNATIONAL SEARCH REPORT

International Application No PCT/EP2004/053573

A. CLASSII IPC 7	FICATION OF SUBJECT MATTER G01N33/68		
	International Patent Classification (IPC) or to both national classifica	tion and IPC	
B. FIELDS		n numbols)	
Minimum do IPC 7	cumentation searched (classification system followed by classificatio $601N$	n symbols)	ļ
Documentat	ion searched other than minimum documentation to the extent that su	uch documents are included in the fields se	arched
Electronic d	ata base consulted during the international search (name of data bas	e and, where practical, search terms used)	
EPO-In	ternal, BIOSIS, EMBASE, FSTA, WPI Da	ata, PAJ	
C. DOCUM	ENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the rele	evant passages	Relevant to claim No.
γ	YUICHI MAKINO ET AL: "Inhibitory	/ PAS	1,2,8,
ļ <b>'</b>	domain protein (IPAS) is a		11,12,
į	hynoxia-inducible splicing variar	nt of the	14-16
	hypoxia-inducible factor-3 alpha	locus"	
	JOURNAL OF BIOLOGICAL CHEMISTRY,	AMERICAN	
Į.	SOCIETY OF BIOLOGICAL CHEMISTS, E	BALIIMURE,	
ĺ	MD, US,		•
ŀ	vol. 277, no. 36,		
	September 2002 (2002-09), pages 32405-32408, XP002960907		
	ISSN: 0021-9258		
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	l and a second and	Patent family members are listed in	n anney
	her documents are listed in the continuation of box C.	Patent lating members are listed to	
1 '	ategories of cited documents :	"T" later document published after the inte or priority date and not in conflict with	rnational filing date the application but
"A" docum	ent defining the general state of the art which is not dered to be of particular relevance	cited to understand the principle or the invention	eory underlying the
"E" earlier	document but published on or after the international	"X" document of particular relevance; the c cannot be considered novel or cannot	laimed invention
"L" docume	ent which may throw doubts on priority claim(s) or	involve an inventive step when the do	cument is taken alone
which citatio	is cited to establish the publication date of another on or other special reason (as specified)	"Y" document of particular relevance; the cannot be considered to involve an in	ventive step when the
	ent referring to an oral disclosure, use, exhibition or means	document is combined with one or mo ments, such combination being obvio	ore other such docu- us to a person skilled
"P" docum	ent published prior to the International filing date but han the priority date claimed	in the art. "&" document member of the same patent	family
1	actual completion of the international search	Date of mailing of the international sea	rch report
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	l3 April 2005	₩ 3. UU.	FAAA
Name and	mailing address of the ISA	Authorized officer	
1	European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk		
	Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Hinchliffe, P	

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# INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP2004/053573

Y HARA S ET AL: "Expression and characterization of hypoxia-inducible factor (HIF)-3 alpha in human kidney: suppression of HIF-mediated gene expression by HIF-3alpha" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS, SAN DIEGO, CA, US, vol. 287, 5 October 2001 (2001-10-05), pages 808-813, XP002221230 ISSN: 0006-291X X the whole document  Y BAZAN N G ET AL: "HYPOXIA SIGNALING TO GENES SIGNIFICANCE IN ALZHEIMER'S DISEASE" MOLECULAR NEUROBIOLOGY, HUMANA PRESS, US, vol. 26, no. 2/3, October 2002 (2002-10), pages 283-298, XP009029127 ISSN: 0893-7648 the whole document  A GU Y-Z ET AL: "MOLECULAR CHARACTERIZATION AND CHROMOSOMAL LOCALIZATION OF A THIRD ALPHA-CLASS HYPOXIA INDUCIBLE FACTOR SUBUNIT, HIF3ALPHA"	3,10 1,2,8, 11,12, 14-16  1-16
characterization of hypoxia-inducible factor (HIF)-3 alpha in human kidney: suppression of HIF-mediated gene expression by HIF-3alpha" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, ACADEMIC PRESS, SAN DIEGO, CA, US, vol. 287, 5 October 2001 (2001-10-05), pages 808-813, XP002221230 ISSN: 0006-291X the whole document  Y BAZAN N G ET AL: "HYPOXIA SIGNALING TO GENES SIGNIFICANCE IN ALZHEIMER'S DISEASE" MOLECULAR NEUROBIOLOGY, HUMANA PRESS, US, vol. 26, no. 2/3, October 2002 (2002-10), pages 283-298, XP009029127 ISSN: 0893-7648 the whole document  A GU Y-Z ET AL: "MOLECULAR CHARACTERIZATION AND CHROMOSOMAL LOCALIZATION OF A THIRD ALPHA-CLASS HYPOXIA INDUCIBLE FACTOR SUBUNIT, HIF3ALPHA"	3,10 1,2,8, 11,12, 14-16
pages 808-813, XP002221230 ISSN: 0006-291X the whole document  PAZAN N G ET AL: "HYPOXIA SIGNALING TO GENES SIGNIFICANCE IN ALZHEIMER'S DISEASE" MOLECULAR NEUROBIOLOGY, HUMANA PRESS, US, vol. 26, no. 2/3, October 2002 (2002-10), pages 283-298, XP009029127 ISSN: 0893-7648 the whole document  A GU Y-Z ET AL: "MOLECULAR CHARACTERIZATION AND CHROMOSOMAL LOCALIZATION OF A THIRD ALPHA-CLASS HYPOXIA INDUCIBLE FACTOR SUBUNIT, HIF3ALPHA"	1,2,8, 11,12, 14-16
GENES SIGNIFICANCE IN ALZHEIMER'S DISEASE" MOLECULAR NEUROBIOLOGY, HUMANA PRESS, US, vol. 26, no. 2/3, October 2002 (2002-10), pages 283-298, XP009029127 ISSN: 0893-7648 the whole document  GU Y-Z ET AL: "MOLECULAR CHARACTERIZATION AND CHROMOSOMAL LOCALIZATION OF A THIRD ALPHA-CLASS HYPOXIA INDUCIBLE FACTOR SUBUNIT, HIF3ALPHA"	11,12, 14-16
AND CHROMOSOMAL LOCALIZATION OF A THIRD ALPHA-CLASS HYPOXIA INDUCIBLE FACTOR SUBUNIT, HIF3ALPHA"	1-16
GENE EXPRESSION, CHICAGO MEDICAL SCHOOL PRESS, NORTH CHICAGO, IL, US, vol. 7, 1998, pages 205-213, XP009000521 ISSN: 1052-2166	